

AMENDMENTS TO THE CLAIMS

Please amend the claims as follows.

Please add new claim 91.

1-23. (canceled)

24. (currently amended) A method for making an aqueous solution of metronidazole greater than 0.75% w/w comprising combining metronidazole, beta-cyclodextrin (BCD), and niacin or niacinamide in ~~water~~ an aqueous fluid.

25. (currently amended) The method of claim 24 wherein the metronidazole is added to the ~~water~~ aqueous fluid after the BCD and the niacin or niacinamide are dissolved in the ~~water~~ aqueous fluid.

26. (original) The method of claim 24 which further comprises, after the combination of metronidazole, BCD, and the niacin or niacinamide, adding a gelling agent.

27. (original) The method of claim 24 wherein niacinamide but not niacin is combined.

28. (original) The method of claim 24 wherein niacin but not niacinamide is combined.

29. (original) An aqueous solution that is made by the method of claim 24.
30. (original) An aqueous solution that is made by the method of claim 26.
31. (original) An aqueous solution that is made by the method of claim 27.
32. (original) An aqueous solution that is made by the method of claim 28.
33. (original) A method for the treatment of a dermatologic or mucosal disorder comprising topically applying an effective amount of aqueous solution of metronidazole having a concentration higher than 0.75% w/w to the site of the disorder and permitting the metronidazole to treat the disorder, wherein the solution comprises beta-cyclodextrin (BCD) and niacin or niacinamide.
34. (original) The method of claim 33 wherein the concentration of metronidazole is about 1% or higher.
35. (original) The method of claim 34 wherein the application is once daily.
36. (original) The method of claim 33 wherein the disorder is rosacea.

37. (original) The method of claim 33 wherein the solution comprises niacin and is substantially free of niacinamide.

38. (original) The method of claim 33 wherein the solution comprises niacinamide and is substantially free of niacin.

39. (original) The method of claim 33 wherein the aqueous solution is a gel.

40. (previously presented) A kit for the topical treatment of dermatologic or mucosal disorders comprising a container and an aqueous solution of metronidazole, beta-cyclodextrin, and niacin or niacinamide within said container, wherein the concentration of metronidazole in said solution is higher than 0.75% w/w.

41. (previously presented) The kit of claim 40 wherein the concentration of metronidazole is about 1% w/w or higher.

42. (original) The kit of claim 40 wherein the aqueous solution is a gel.

43. (original) The kit of claim 40 wherein the solution contains niacinamide and is substantially free of niacin.

44. (original) The kit of claim 40 wherein the solution contains niacin and is substantially free of niacinamide.

45. (amended) An aqueous solution that is physically stable for at least one week at 5°C comprising metronidazole, a first solubility enhancing agent which is betacyclodextrin, and a second solubility enhancing agent which is niacin or niacinamide.

46. (previously presented) The aqueous solution of claim 45 wherein the solubility enhancing agent is niacinamide.

47. (currently amended) The aqueous solution of claim 45 wherein the solubility enhancing agent is niacin.

48. (previously presented) The aqueous solution of claim 45 wherein the concentration of metronidazole in the solution is higher than 0.75% w/w.

49. (previously presented) The aqueous solution of claim 48 wherein the concentration of metronidazole is about 1.0% or higher.

50. (previously presented) The aqueous solution of claim 48 wherein the solubility enhancing agent is niacinamide.

51. (previously presented) The aqueous solution of claim 48 wherein the solubility enhancing agent is niacin.

52. (currently amended) The aqueous solution of claim 45 wherein in the solution, the concentration of metronidazole is about 1.0% w/w or higher, the concentration of betacyclodextrin is about ~~1.0%~~ 0.5% w/w or ~~less~~ higher, and the concentration of niacinamide or niacin is about 0.5% w/w or ~~more~~ higher.

53. (previously presented) The aqueous solution of claim 52 which comprises niacinamide and does not comprise niacin.

54. (previously presented) The aqueous solution of claim 52 wherein the concentration of niacinamide or niacin is about 1.0% w/w or higher.

55. (previously presented) The aqueous solution of claim 54 which comprises niacinamide and does not comprise niacin.

56. (previously presented) The aqueous solution of claim 46 wherein the concentration of niacinamide in the solution is below that which, in the absence of betacyclodextrin, increases the water solubility of metronidazole to the concentration of metronidazole present in the solution.

57. (previously presented) The aqueous solution of claim 47 wherein the concentration of niacin in the solution is below that which, in the absence of betacyclodextrin, increases the water solubility of metronidazole to the concentration of metronidazole present in the solution.

58. (previously presented) The aqueous solution of claim 45 wherein the concentration of betacyclodextrin in the solution is below that which, in the absence of niacinamide or niacin, increases the water solubility of metronidazole to the concentration of metronidazole present in the solution.

59. (previously presented) The aqueous solution of claim 45 which is a gel.

60. (previously presented) The aqueous solution of claim 48 which is a gel.

61. (previously presented) The aqueous solution of claim 50 which is a gel.

62. (previously presented) The aqueous solution of claim 51 which is a gel.

63. (previously presented) A method for increasing the solubility of metronidazole in aqueous solution comprising combining metronidazole, betacyclodextrin, and niacinamide or niacin in an aqueous fluid.

64. (previously presented) The method of claim 63 wherein the aqueous solution is a gel.

65. (previously presented) The method of claim 63 which comprises combining niacinamide in the fluid.

66. (previously presented) The method of claim 63 which comprises combining niacin in the fluid.

67. (previously presented) The method of claim 63 wherein the solubility of metronidazole is increased to 0.75% w/w or more.

68. (previously presented) The method of claim 67 wherein the solubility of metronidazole is increased to about 1.0% w/w or more.

69. (previously presented) The method of claim 63 wherein the betacyclodextrin and the niacin and niacinamide are dissolved in the aqueous fluid before the metronidazole is combined in the fluid.

70. (previously presented) The method of claim 63 wherein a gelling agent is added to the fluid after the metronidazole, betacyclodextrin, and the niacin or niacinamide are combined in the fluid.

71. (previously presented) The method of claim 63 wherein the amount of niacinamide or niacin that is combined in the fluid is below that which, in the absence of betacyclodextrin, increases the water solubility of metronidazole to the concentration of metronidazole that is soluble in the solution.

72. (previously presented) The method of claim 63 wherein the amount of betacyclodextrin in the solution that is combined in the fluid is below that which, in the absence of niacinamide or niacin, increases the water solubility of metronidazole to the concentration of metronidazole that is soluble in the solution.

73. (previously presented) The method of claim 63 wherein the amount of niacinamide or niacin that is combined in the fluid is below that which, in the absence of betacyclodextrin, increases the water solubility of metronidazole to the concentration of metronidazole that is soluble in the solution, and the amount of betacyclodextrin in the solution that is combined in the fluid is below that which, in the absence of niacinamide or niacin, increases the water solubility of metronidazole to the concentration of metronidazole that is soluble in the solution.

74. (previously presented) A method for increasing the enhancing effect of betacyclodextrin on the solubility of metronidazole in aqueous fluid comprising combining niacin or niacinamide with the betacyclodextrin in the aqueous fluid.

75. (previously presented) The method of claim 74 wherein the niacin or niacinamide is combined in the fluid with the betacyclodextrin and then metronidazole is added to the fluid.

76. (previously presented) The method of claim 74 wherein niacin is combined with the betacyclodextrin in the aqueous fluid.

77. (previously presented) The method of claim 74 wherein niacinamide is combined with the betacyclodextrin in the aqueous fluid.

78. (currently amended) The method of claim 74 wherein the concentration of betacyclodextrin in the fluid is about ~~1.0% or less~~ 0.5% or more and the concentration of niacin or niacinamide is about 0.5% w/w or more.

79. (previously presented) The method of claim 78 wherein the concentration of niacin or niacinamide is about 1.0% or more.

80. (previously presented) The method of claim 24 wherein the betacyclodextrin is crystalline betacyclodextrin.

81. (previously presented) An aqueous solution that is made by the method of claim 80.

82. (currently amended) An aqueous solution comprising betacyclodextrin at a ~~concentration greater than 0.5 % w/w and niacinamide, wherein the solution is free of crystal or precipitate formation when stored for one week at 5°C.~~

83. (currently amended) The aqueous solution of claim 82 wherein the concentration of betacyclodextrin is about 1% w/w or higher.

84. (currently amended) The aqueous solution of claim 82 wherein the ~~aqueous solution further comprises niacinamide~~ concentration of betacyclodextrin is greater than 0.5 % w/w.

85. (previously presented) The aqueous solution of claim 82 wherein the aqueous solution further comprises metronidazole.

86. (currently amended) The aqueous solution of claim 82 84 which ~~wherein the aqueous solution~~ further comprises ~~niacinamide and~~ metronidazole.

87. (canceled)

88. (previously presented) The aqueous solution of claim 82 which is an aqueous gel solution.

89. (currently amended) A method for obtaining an aqueous solution containing betacyclodextrin at a concentration greater than 0.5% w/w comprising combining in ~~water~~ an aqueous fluid betacyclodextrin and niacinamide wherein the amount of the niacinamide combined in the ~~water~~ aqueous fluid is sufficient to provide a dissolved concentration of betacyclodextrin greater than 0.5% w/w at a temperature of 5°C.

90. (previously presented) The method of claim 89 wherein the aqueous solution containing betacyclodextrin at a concentration greater than 0.5% w/w and niacinamide is physically stable for one week at 5°C.

91. (new) The method of claim 89 wherein the aqueous solution is an aqueous gel solution.